☐ 1: J Immunol 1996 May 15;156(10):3911-8

Enhanced tumor outgrowth after peptide vaccination. Functional deletion of tumor-specific CTL induced by peptide vaccination can lead to the inability to reject tumors.

Toes RE, Blom RJ, Offringa R, Kast WM, Melief CJ.

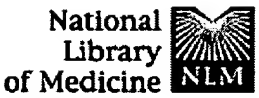
Department of Immunohematology and Blood Bank, University Hospital, Leiden, The Netherlands.

CTL can play an important role in the defense against tumors. Protective CTL-mediated immunity can be established in animal tumor models after vaccination with synthetic peptides representing CTL epitopes. We now report that immunization with synthetic peptides can also lead to CTL tolerance associated with the inability to reject tumors. B6 tumor cells transformed by the human adenovirus early region 1 (Ad5E1) present an Ad5E1A- and an Ad5E1B-encoded CTL epitope to the immune system. CTL clones directed against either of these epitopes are able to eradicate established Ad5E1-induced tumors, showing that these CTL epitopes are targets of CTL that can mediate tumor regression. Here, we show that protective immunity against Ad5E1-expressing tumor cells can be established by immunization with Ad5E1-transformed cells and with an adenovirus vector containing the Ad5E1 region. Protective immunity, in either case, is associated with specific CTL memory. To test whether vaccination with synthetic peptides leads to protection against Ad5E1-expressing tumor cells, we vaccinated mice s.c. with a low dose of the Ad5E1B peptide. This peptide was chosen because the CTL response against the Ad5E1B-encoded CTL epitope contributes most to the antitumor response in B6 mice after vaccination with Ad5E1-transformed cells. Ad5E1B peptide-vaccinated mice were not protected against the outgrowth of Ad5E1-expressing tumor cells, but instead were no longer able to reject a tumor

down-loaded full journal article

inoculum that was rejected by nonvaccinated mice. Moreover, the protection induced by tumor cell vaccination against Ad5E1B-expressing tumors was gone when the Ad5E1B-encoded CTL epitope was injected a few days before tumor challenge. This is associated with peptide-induced tolerance of Ad5E1B-specific CTL activity. These findings are relevant for the design of therapeutic approaches against both malignancies and T cell-mediated autoimmune diseases.

PMID: 8621930 [PubMed - indexed for MEDLINE]



About Entrez

Text Version

Entrez PubMed
Overview
Help | FAQ
Tutorial
New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Browser
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
LinkOut
Cubby

Related Resources
Order Documents
NLM Gateway
TOXNET
Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

Privacy Policy

- Search History will be lost after one hour of inactivity.
- To combine searches use # before search number, e.g., #2 AND #6.
- Search numbers may not be continuous; all searches are represented.

Search	Most Recent Queries	Time	Result
#3	Related Articles for PubMed (Select 10402230)	10:53:55	173
#1	Search tumor burden AND autologous apcs Field: All Fields	10:52:24	1

Clear History

Write to the Help Desk
NCBI | NLM | NIH
Department of Health & Human Services
Freedom of Information Act | Disclaimer

i686-pc-linux-gnu Oct 21 2002 11:24:19

Search09781023
Your SELECT statement is:
s neuroblastoma and apc

Items	File
16	5: Biosis Previews(R)_1969-2002/Oct W3
26	34: SciSearch(R) Cited Ref Sci_1990-2002/Oct W4
6	71: ELSEVIER BIOBASE_1994-2002/Oct W3
8	73: EMBASE_1974-2002/Oct W3
4	94: JICST-EPlus_1985-2002/Aug W3
2	98: General Sci Abs/Full-Text_1984-2002/Sep
6	144: Pascal_1973-2002/Oct W3
5	149: TGG Health&Wellness DB(SM)_1976-2002/Oct W2
12	155: MEDLINE(R)_1966-2002/Oct W3
2	156: ToxFile_1965-2002/Oct W3
13	159: Cancerlit_1975-2002/Sep
2	266: FEDRIP_2002/Aug
1	370: Science_1996-1999/Jul W3
8	399: CA SEARCH(R)_1967-2002/UD=13717
2	442: AMA Journals_1982-2002/Oct B2
1	444: New England Journal of Med._1985-2002/Oct W4

SYSTEM:OS - DIALOG OneSearch
File 5:Biosis Previews(R) 1969-2002/Oct W3
(c) 2002 BIOSIS
*File 5: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.
File 34:SciSearch(R) Cited Ref Sci 1990-2002/Oct W4
(c) 2002 Inst for Sci Info
*File 34: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.
File 155:MEDLINE(R) 1966-2002/Oct W3
*File 155: Alert feature enhanced for multiple files, duplicates removal, customized scheduling. See HELP ALERT.
File 159:Cancerlit 1975-2002/Sep
(c) format only 2002 Dialog Corporation
4/9/1 (Item 1 from file: 5)
DIALOG(R)File 5:Biosis Previews(R)

13104172 BIOSIS NO.: 200100311321
T-cells with specificity against neuroblastoma cells activated by dendritic cells.
AUTHOR: Klein-Franke A(a); Ertle F(a); Berkutzky T(a); Peters H
AUTHOR ADDRESS: (a)Pediatrics, University, Goettingen**Germany
JOURNAL: Blood 96 (11 Part 2):p41b November 16, 2000

MEDIUM: print
CONFERENCE/MEETING: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000
SPONSOR: American Society of Hematology
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English
SUMMARY LANGUAGE: English

ABSTRACT: Introduction: Neuroblastoma is the most frequent solid tumor in children with a poor prognosis despite intensive, multimodal therapy. To improve the outcome new therapeutic approaches are necessary. One new approach in tumor therapy is the activation of cytotoxic T-cells against tumor cells by Dendritic Cells which are by far the most effective Antigen Presenting Cells (APC). Materials and Methods: We used the Neuroblastoma line SK-N-LO and buffy coats of HLA-I matched blood donors as a source for monocytes and T-cells. We isolated the monocytes by plastic adherence and differentiated them into DC by cultivation in the presence of GM-CSF and IL 4 (100 U/ml) and IFN gamma (50 U/ml) for 8 days. Mixed Tumor/Lymphocyte Culture (MLTC) was performed using DC as APC that had either been pulsed with tumor cell lysate or fused to tumor cells by PEG. T-cell proliferation was assessed by 3H-Thymidin incorporation and the cytotoxicity of T-cells was monitored via LDH release from tumor cells (4 hours cocultivation, effector:target ratio 10:1). Results: Without DC no activation of T-cells could be seen. In the presence of DC pulsed with tumor cell lysate T-cells were activated leading to a 3H-Thymidin incorporation of 3100 cpm. T-cell activation by DC/tumor cell hybrids was even more efficient yielding 6400 cpm. In both cases CD8+T-cells were selected and could be kept in continous culture by restimulation with manipulated DC every 14 days, followed by culture in the presence of IL2 for up to four cycles. Freshly activated T-cells lysed 43% of the Neuroblastoma cells, Neuroblastoma cells with different HLA-I formula were not lysed, nor were K562 cells. Lysis of tumor cells was abrogated by a polyclonal rat antibody specific for HLA-I, thus demonstrating the tumor cell lysis to be HLA-I restricted. Discussion: We could activate cytotoxic T-cells against Neuroblastoma cells using Dendritic Cells as APC . Hybrids of DC and tumor cells were even more effective. Target cell lysis was antigen specific, thus the Neuroblastoma cells can be expected to to have tumor associated antigens. Activated T-cells killed Neuroblastoma cells in a HLA-I depentent manner. This is particularly interesting as Neuroblastoma cells bear only very small amounts of HLA-I molecules on their surface. Despite of this Neuroblastoma cells are obviously a suitable target for activated T-cells. These results could lead to clinical studies in the therapy of Neuroblastoma using DC for the activation of tumor specific T-cells.